

Amendments to the Specification:

Please replace paragraph [0091] beginning at page 34, line 22, with the following:

[0091] Particular IMSs of the invention comprise the following hexamer sequences:

1. 5'-purine-pyrimidine-[X]-[Y]-pyrimidine-pyrimidine-3' IMSs containing GG dinucleotide cores: GTGGTT (SEQ ID NO:1), ATGGTT (SEQ ID NO:2), GCGGTT (SEQ ID NO:3), ACGGTT (SEQ ID NO:4), GTGGCT (SEQ ID NO:5), ATGGCT (SEQ ID NO:6), GCGGCT (SEQ ID NO:7), ACGGCT (SEQ ID NO:8), GTGGTC (SEQ ID NO:9), ATGGTC (SEQ ID NO:10), GCGGTC (SEQ ID NO:11), ACGGTC (SEQ ID NO:12), and so forth;
2. 5'-purine-pyrimidine-[X]-[Y]-pyrimidine-pyrimidine-3' IMSs containing GC dinucleotides cores: GTGCTT (SEQ ID NO:13), ATGCTT (SEQ ID NO:14), GCGCTT (SEQ ID NO:15), ACGCTT (SEQ ID NO:16), GTGCCT (SEQ ID NO:17), ATGCCT (SEQ ID NO:18), GCGCCT (SEQ ID NO:19), ACGCCT (SEQ ID NO:20), GTGCTC (SEQ ID NO:21), ATGCTC (SEQ ID NO:22), GCGCTC (SEQ ID NO:23), ACGCTC (SEQ ID NO:24), and so forth;
3. Guanine and inosine substitutes for adenine and/or uridine substitutes for cytosine or thymine and those substitutions can be made as set forth based on the guidelines above.

Please replace paragraph [0092] beginning at page 35, line 4, with the following:

[0092] A previously disclosed immune inhibitory sequence or IIS, was shown to inhibit immunostimulatory sequences (ISS) activity containing a core dinucleotide, CpG. U.S. Patent 6,225,292. This IIS, in the absence of an ISS, was shown for the first time by this invention to prevent and treat autoimmune disease either alone or in combination with DNA polynucleotide therapy. This IIS contained the core hexamer region having the sequence AAGGTT. That

sequence is referred to herein as an immune modulatory sequence or IMS. Other related IISs with a similar motif included within the IMSs of this invention are:

1. 5'-purine-purine-[X]-[Y]-pyrimidine-pyrimidine-3' IMSs containing GG dinucleotide cores: GGGGTT (SEQ ID NO:25), AGGGTT (SEQ ID NO:26), GAGGTT (SEQ ID NO:27), AAGGTT (SEQ ID NO:28), GGGGCT (SEQ ID NO:29), AGGGCT (SEQ ID NO:30), GAGGCT (SEQ ID NO:31), AAGGCT (SEQ ID NO:32), GGGGTC (SEQ ID NO:33), AGGGTC (SEQ ID NO:34), GAGGTC (SEQ ID NO:35), AAGGTC (SEQ ID NO:36), and so forth;
2. 5'-purine-purine-[X]-[Y]-pyrimidine-pyrimidine-3' IMSs containing GC dinucleotide cores: GGGCTT (SEQ ID NO:37), AGGCTT (SEQ ID NO:38), GAGCTT (SEQ ID NO:39), AAGCTT (SEQ ID NO:40), GGGCCT (SEQ ID NO:41), AGGCCT (SEQ ID NO:42), GAGCCT (SEQ ID NO:43), AAGCCT (SEQ ID NO:44), GGGCTC (SEQ ID NO:45), AGGCTC (SEQ ID NO:46), GAGCTC (SEQ ID NO:47), AAGCTC (SEQ ID NO:48), and so forth;
3. Guanine and inosine substitutions for adenine and/or uridine substitutions for cytosine or thymine can be made as set forth based on the guidelines above.

Please replace paragraph [0130] beginning at page 47, line 20, with the following:

[0130] Stimulatory CpG-ODN is known to activate immune cells derived from spleens including dendritic cells, macrophages, T cells, and B cells (*see*, Krieg et. al., *Nature*, 374:546-549, 1995; Yi et. al., *J. Immunol.*, 157:5394-5402, 1996; Klinman et. al., *Proc Nat. Acad. Sci. USA*, 93:2879-2883, 1996; Martin-Orozco et. al., *Int. Immunol.*, 11:1111-1118, 1999; Sparwasser et. al., *Eur. J. Immunol.*, 28:2045-2054, 1998). The effects of IMS were assessed by measuring overall proliferation of naïve splenocytes. We constructed a 22-mer oligonucleotide sequence containing a single 5'-AACGTT-3' (CpG-ODN) (SEQ ID NO:49) or an IMS 5'-AAGGTT-3' (SEQ ID NO:50) sequence with a phosphorothioate backbone to protect the DNA

from nuclease degradation. To determine whether the addition of the IMS would counteract the effects of stimulatory CpG-ODN, isolated naïve whole splenocytes were cultured with 5 µg/ml stimulatory CpG-ODN alone and with increasing concentrations of IMS. After 48 hrs whole splenocyte proliferation decreased 2-fold upon the addition of 1 µg/ml IMS, and decreased 3-fold with the addition of 5 µg/ml and 10 µg/ml of IMS (Figure 1A).

Please replace paragraph [0178] beginning at page 62, line 30, with the following:

[0178] The efficacy of IMS treatment alone and in combination with DNA encoding the self-proteins dihydrolipoamide acetyl-transferase (E2) and E3-binding protein components of the PDC was tested in SJL/J female mice. Groups of 15 eight-week-old female SJL/J mice were injected intramuscularly (IM) in both quadriceps with a total of 0.2ml 0.25% Bupivacaine-HCL in PBS. Two days later, mice were injected intramuscularly in both quadriceps with 50 µg/dose of each of the indicated DNA vaccines (pTarget plasmid, PDC-E2 in pTarget, and the combination of PDC-E2 and IL4) with three weekly doses. At the same time as initial DNA vaccination, 50 µg IMS or CpG in a volume of 200 µl PBS was administered intraperitoneally alone or with DNA vaccination. Mice were induced with PDC-E2 peptide GDLLAEIETDKATI (SEQ ID NO:51) (500 µg in 100 µl PBS) emulsified 1:1 (v/v) with CFA (containing 10 mg/ml *Mycobacterium tuberculosis* strain H37RA) with a single 200 µl intraperitoneal injection. EAC is assessed 30 weeks after sensitization. H&E stained liver sections is used for morphologic assessment of necroinflammation and bile duct injury.

Please replace paragraph [0180] beginning at page 63, line 15, to insert the SEQ ID NOs with the following:

[0180] It is predicted that additional IMS oligonucleotides will have similar or improved efficacy in altering the course of autoimmune disease. The sequence of these additional IMS oligonucleotides are based on the efficacy data obtained with the IMS oligonucleotide described

earlier (*i.e.*, 5'-TGACTGTGAAGGTTAGAGATGA-3' (SEQ ID NO:52)). Additional IMS oligonucleotides predicted to have similar or improved efficacy follow the following pattern: 5'-TGACTGTGTGRR $\alpha\beta$ YYAGAGATGA-3' (SEQ ID NO:53), where R represent purines (A or G), Y represent pyrimidines (C or T), and α and β are either GpG or non-GpG dinucleotides. These oligonucleotides are predicted to have the most robust efficacy in rodent assays as the consensus follows what has been reported to be most active in rodent systems. A complete list of these IMS oligonucleotides are listed in Table 4. In the table, "I" represents inosine.

Please replace paragraph [0181] beginning at page 63, line 26, to insert the SEQ ID NOs with the following::

[0181] Similarly, additional IMS oligonucleotides predicted to have similar or improved efficacy follow the following pattern: 5'-TGACTGTGTGRY $\alpha\beta$ YYAGAGATGA-3' (SEQ ID NO:54) where R represent purines (A or G), Y represent pyrimidines (C or T), and α and β are either GpG or non-GpG dinucleotides. These oligonucleotides are predicted to have the most robust efficacy in human assays as the consensus follows what has been reported to be most active in human systems. A complete list of these IMS oligonucleotides are listed in Table 5. In the table, "I" represents inosine.

Please replace paragraph [0183] beginning at page 64, line 10, to insert the SEQ ID NOs with the following::

[0183] In both Table 4 and Table 5, examples of both 5' and 3' flanking sequences around the core hexamer (*i.e.*, RR $\alpha\beta$ YY or RY $\alpha\beta$ YY) are depicted. Additional flanking sequences surrounding this core hexamer are created by substituting the flanking sequences with any nucleotide sequence of any length. This is represented in the following sequences:

5'-NNNNNNNNNNR α β YYNNNNNNNNN-3' and 5'-(SEQ ID NO:55)-
 NNNNNNNNNNR α β YYNNNNNNNNN-3' (SEQ ID NO:56), where N represents any
 nucleotide. Specific examples include, but are not limited to, the following oligonucleotides:

5'-GGGGGGGGGAAGGTTGGGGGGGGG-3' (SEQ ID NO:57),
 5'-GGGGGGGGGATGGTTGGGGGGGGG-3' (SEQ ID NO:58),
 5'-GGGGGGGGGACGGTTGGGGGGGGG-3' (SEQ ID NO:59),
 5'-GGGGGGGGGAAGCTTGGGGGGGGG-3' (SEQ ID NO:60),
 5'-GGGGGGGGGATGCTTGGGGGGGGG-3' (SEQ ID NO:61),
 5'-GGGGGGGGGACGCTTGGGGGGGGG-3' (SEQ ID NO:62),
 5'-CCCCCCCCCAAGGTTCCCCCCCCC-3' (SEQ ID NO:63),
 5'-CCCCCCCCCATGGTTCCCCCCCCC-3' (SEQ ID NO:64),
 5'-CCCCCCCCCACGTTCCCCCCCCC-3' (SEQ ID NO:65),
 5'-CCCCCCCCCAAGCTTCCCCCCCCC-3' (SEQ ID NO:66),
 5'-CCCCCCCCCATGCTTCCCCCCCCC-3' (SEQ ID NO:67),
 5'-CCCCCCCCCACGCTTCCCCCCCCC-3' (SEQ ID NO:68).

TABLE 4

5'	R	R	α	β	Y	Y	3'
TGACTGTG	A	A	G	C	T	T	AGAGATGA (SEQ ID NO:69)
TGACTGTG	A	A	G	C	T	C	AGAGATGA (SEQ ID NO:70)
TGACTGTG	A	A	G	C	C	T	AGAGATGA (SEQ ID NO:71)
TGACTGTG	A	A	G	C	C	C	AGAGATGA (SEQ ID NO:72)
TGACTGTG	A	G	G	C	T	T	AGAGATGA (SEQ ID NO:73)
TGACTGTG	A	G	G	C	T	C	AGAGATGA (SEQ ID NO:74)
TGACTGTG	A	G	G	C	C	T	AGAGATGA (SEQ ID NO:75)
TGACTGTG	A	G	G	C	C	C	AGAGATGA (SEQ ID NO:76)
TGACTGTG	G	A	G	C	T	T	AGAGATGA (SEQ ID NO:77)
TGACTGTG	G	A	G	C	T	C	AGAGATGA (SEQ ID NO:78)
TGACTGTG	G	A	G	C	C	T	AGAGATGA (SEQ ID NO:79)
TGACTGTG	G	A	G	C	C	C	AGAGATGA (SEQ ID NO:80)

5'	R	R	α	β	Y	Y	3'
TGACTGTG	G	G	G	C	T	T	AGAGATGA (SEQ ID NO:81)
TGACTGTG	G	G	G	C	T	C	AGAGATGA (SEQ ID NO:82)
TGACTGTG	G	G	G	C	C	T	AGAGATGA (SEQ ID NO:83)
TGACTGTG	G	G	G	C	C	C	AGAGATGA (SEQ ID NO:84)
TGACTGTG	A	A	G	G	T	T	AGAGATGA (SEQ ID NO:85)
TGACTGTG	A	A	G	G	T	C	AGAGATGA (SEQ ID NO:86)
TGACTGTG	A	A	G	G	C	T	AGAGATGA (SEQ ID NO:87)
TGACTGTG	A	A	G	G	C	C	AGAGATGA (SEQ ID NO:88)
TGACTGTG	A	G	G	G	T	T	AGAGATGA (SEQ ID NO:89)
TGACTGTG	A	G	G	G	T	C	AGAGATGA (SEQ ID NO:90)
TGACTGTG	A	G	G	G	C	T	AGAGATGA (SEQ ID NO:91)
TGACTGTG	A	G	G	G	C	C	AGAGATGA (SEQ ID NO:92)
TGACTGTG	G	A	G	G	T	T	AGAGATGA (SEQ ID NO:93)
TGACTGTG	G	A	G	G	T	C	AGAGATGA (SEQ ID NO:94)
TGACTGTG	G	A	G	G	C	T	AGAGATGA (SEQ ID NO:95)
TGACTGTG	G	A	G	G	C	C	AGAGATGA (SEQ ID NO:96)
TGACTGTG	G	G	G	G	T	T	AGAGATGA (SEQ ID NO:97)
TGACTGTG	G	G	G	G	T	C	AGAGATGA (SEQ ID NO:99)
TGACTGTG	G	G	G	G	C	T	AGAGATGA (SEQ ID NO:99)
TGACTGTG	G	G	G	G	C	C	AGAGATGA (SEQ ID NO:100)
TGACTGTG	A	A	A	G	T	T	AGAGATGA (SEQ ID NO:101)
TGACTGTG	A	A	A	G	T	C	AGAGATGA (SEQ ID NO:102)
TGACTGTG	A	A	A	G	C	T	AGAGATGA (SEQ ID NO:103)
TGACTGTG	A	A	A	G	C	C	AGAGATGA (SEQ ID NO:104)
TGACTGTG	A	G	A	G	T	T	AGAGATGA (SEQ ID NO:105)
TGACTGTG	A	G	A	G	T	C	AGAGATGA (SEQ ID NO:106)
TGACTGTG	A	G	A	G	C	T	AGAGATGA (SEQ ID NO:107)

5'	R	R	α	β	Y	Y	3'
TGACTGTG	A	G	A	G	C	C	AGAGATGA (SEQ ID NO:108)
TGACTGTG	G	A	A	G	T	T	AGAGATGA (SEQ ID NO:109)
TGACTGTG	G	A	A	G	T	C	AGAGATGA (SEQ ID NO:110)
TGACTGTG	G	A	A	G	C	T	AGAGATGA (SEQ ID NO:111)
TGACTGTG	G	A	A	G	C	C	AGAGATGA (SEQ ID NO:112)
TGACTGTG	G	G	A	G	T	T	AGAGATGA (SEQ ID NO:113)
TGACTGTG	G	G	A	G	T	C	AGAGATGA (SEQ ID NO:114)
TGACTGTG	G	G	A	G	C	T	AGAGATGA (SEQ ID NO:115)
TGACTGTG	G	G	A	G	C	C	AGAGATGA (SEQ ID NO:116)
TGACTGTG	A	A	I	G	T	T	AGAGATGA (SEQ ID NO:117)
TGACTGTG	A	A	I	G	T	C	AGAGATGA (SEQ ID NO:118)
TGACTGTG	A	A	I	G	C	T	AGAGATGA (SEQ ID NO:119)
TGACTGTG	A	A	I	G	C	C	AGAGATGA (SEQ ID NO:120)
TGACTGTG	A	G	I	G	T	T	AGAGATGA (SEQ ID NO:121)
TGACTGTG	A	G	I	G	T	C	AGAGATGA (SEQ ID NO:122)
TGACTGTG	A	G	I	G	C	T	AGAGATGA (SEQ ID NO:123)
TGACTGTG	A	G	I	G	C	C	AGAGATGA (SEQ ID NO:124)
TGACTGTG	G	A	I	G	T	T	AGAGATGA (SEQ ID NO:125)
TGACTGTG	G	A	I	G	T	C	AGAGATGA (SEQ ID NO:126)
TGACTGTG	G	A	I	G	C	T	AGAGATGA (SEQ ID NO:127)
TGACTGTG	G	A	I	G	C	C	AGAGATGA (SEQ ID NO:128)
TGACTGTG	G	G	I	G	T	T	AGAGATGA (SEQ ID NO:129)
TGACTGTG	G	G	I	G	T	C	AGAGATGA (SEQ ID NO:130)
TGACTGTG	G	G	I	G	C	T	AGAGATGA (SEQ ID NO:131)
TGACTGTG	G	G	I	G	C	C	AGAGATGA (SEQ ID NO:132)
TGACTGTG	A	A	I	C	T	T	AGAGATGA (SEQ ID NO:133)
TGACTGTG	A	A	I	C	T	C	AGAGATGA (SEQ ID NO:134)

5'	R	R	α	β	Y	Y	3'
TGACTGTG	A	A	I	C	C	T	AGAGATGA (SEQ ID NO:135)
TGACTGTG	A	A	I	C	C	C	AGAGATGA (SEQ ID NO:136)
TGACTGTG	A	G	I	C	T	T	AGAGATGA (SEQ ID NO:137)
TGACTGTG	A	G	I	C	T	C	AGAGATGA (SEQ ID NO:138)
TGACTGTG	A	G	I	C	C	T	AGAGATGA (SEQ ID NO:139)
TGACTGTG	A	G	I	C	C	C	AGAGATGA (SEQ ID NO:140)
TGACTGTG	G	A	I	C	T	T	AGAGATGA (SEQ ID NO:141)
TGACTGTG	G	A	I	C	T	C	AGAGATGA (SEQ ID NO:142)
TGACTGTG	G	A	I	C	C	T	AGAGATGA (SEQ ID NO:143)
TGACTGTG	G	A	I	C	C	C	AGAGATGA (SEQ ID NO:144)
TGACTGTG	G	G	I	C	T	T	AGAGATGA (SEQ ID NO:145)
TGACTGTG	G	G	I	C	T	C	AGAGATGA (SEQ ID NO:146)
TGACTGTG	G	G	I	C	C	T	AGAGATGA (SEQ ID NO:147)
TGACTGTG	G	G	I	C	C	C	AGAGATGA (SEQ ID NO:148)
TGACTGTG	A	A	T	G	T	T	AGAGATGA (SEQ ID NO:149)
TGACTGTG	A	A	T	G	T	C	AGAGATGA (SEQ ID NO:150)
TGACTGTG	A	A	T	G	C	T	AGAGATGA (SEQ ID NO:151)
TGACTGTG	A	A	T	G	C	C	AGAGATGA (SEQ ID NO:152)
TGACTGTG	A	G	T	G	T	T	AGAGATGA (SEQ ID NO:153)
TGACTGTG	A	G	T	G	T	C	AGAGATGA (SEQ ID NO:154)
TGACTGTG	A	G	T	G	C	T	AGAGATGA (SEQ ID NO:155)
TGACTGTG	A	G	T	G	C	C	AGAGATGA (SEQ ID NO:156)
TGACTGTG	G	A	T	G	T	T	AGAGATGA (SEQ ID NO:157)
TGACTGTG	G	A	T	G	T	C	AGAGATGA (SEQ ID NO:158)
TGACTGTG	G	A	T	G	C	T	AGAGATGA (SEQ ID NO:159)
TGACTGTG	G	A	T	G	C	C	AGAGATGA (SEQ ID NO:160)
TGACTGTG	G	G	T	G	T	T	AGAGATGA (SEQ ID NO:161)

5'	R	R	α	β	Y	Y	3'
TGACTGTG	G	G	T	G	T	C	AGAGATGA (SEQ ID NO:162)
TGACTGTG	G	G	T	G	C	T	AGAGATGA (SEQ ID NO:163)
TGACTGTG	G	G	T	G	C	C	AGAGATGA (SEQ ID NO:164)
TGACTGTG	A	A	T	A	T	T	AGAGATGA (SEQ ID NO:165)
TGACTGTG	A	A	T	A	T	C	AGAGATGA (SEQ ID NO:166)
TGACTGTG	A	A	T	A	C	T	AGAGATGA (SEQ ID NO:167)
TGACTGTG	A	A	T	A	C	C	AGAGATGA (SEQ ID NO:168)
TGACTGTG	A	G	T	A	T	T	AGAGATGA (SEQ ID NO:169)
TGACTGTG	A	G	T	A	T	C	AGAGATGA (SEQ ID NO:170)
TGACTGTG	A	G	T	A	C	T	AGAGATGA (SEQ ID NO:171)
TGACTGTG	A	G	T	A	C	C	AGAGATGA (SEQ ID NO:172)
TGACTGTG	G	A	T	A	T	T	AGAGATGA (SEQ ID NO:173)
TGACTGTG	G	A	T	A	T	C	AGAGATGA (SEQ ID NO:174)
TGACTGTG	G	A	T	A	C	T	AGAGATGA (SEQ ID NO:175)
TGACTGTG	G	A	T	A	C	C	AGAGATGA (SEQ ID NO:176)
TGACTGTG	G	G	T	A	T	T	AGAGATGA (SEQ ID NO:177)
TGACTGTG	G	G	T	A	T	C	AGAGATGA (SEQ ID NO:178)
TGACTGTG	G	G	T	A	C	T	AGAGATGA (SEQ ID NO:179)
TGACTGTG	G	G	T	A	C	C	AGAGATGA (SEQ ID NO:180)
TGACTGTG	A	A	C	G	T	T	AGAGATGA (SEQ ID NO:181)
TGACTGTG	A	A	C	C	T	T	AGAGATGA (SEQ ID NO:182)

TABLE 5

5'	R	Y	α	β	Y	Y	3'
TGACTGTG	A	T	G	C	T	T	AGAGATGA (SEQ ID NO:183)
TGACTGTG	A	T	G	C	T	C	AGAGATGA (SEQ ID NO:184)

5'	R	Y	α	β	Y	Y	3'	
TGACTGTG	A	T	G	C	C	T	AGAGATGA	(SEQ ID NO:185)
TGACTGTG	A	T	G	C	C	C	AGAGATGA	(SEQ ID NO:186)
TGACTGTG	A	C	G	C	T	T	AGAGATGA	(SEQ ID NO:187)
TGACTGTG	A	C	G	C	T	C	AGAGATGA	(SEQ ID NO:188)
TGACTGTG	A	C	G	C	C	T	AGAGATGA	(SEQ ID NO:189)
TGACTGTG	A	C	G	C	C	C	AGAGATGA	(SEQ ID NO:190)
TGACTGTG	G	T	G	C	T	T	AGAGATGA	(SEQ ID NO:191)
TGACTGTG	G	T	G	C	T	C	AGAGATGA	(SEQ ID NO:192)
TGACTGTG	G	T	G	C	C	T	AGAGATGA	(SEQ ID NO:193)
TGACTGTG	G	T	G	C	C	C	AGAGATGA	(SEQ ID NO:194)
TGACTGTG	G	C	G	C	T	T	AGAGATGA	(SEQ ID NO:195)
TGACTGTG	G	C	G	C	T	C	AGAGATGA	(SEQ ID NO:196)
TGACTGTG	G	C	G	C	C	T	AGAGATGA	(SEQ ID NO:197)
TGACTGTG	G	C	G	C	C	C	AGAGATGA	(SEQ ID NO:198)
TGACTGTG	A	T	G	G	T	T	AGAGATGA	(SEQ ID NO:199)
TGACTGTG	A	T	G	G	T	C	AGAGATGA	(SEQ ID NO:200)
TGACTGTG	A	T	G	G	C	T	AGAGATGA	(SEQ ID NO:201)
TGACTGTG	A	T	G	G	C	C	AGAGATGA	(SEQ ID NO:202)
TGACTGTG	A	C	G	G	T	T	AGAGATGA	(SEQ ID NO:203)
TGACTGTG	A	C	G	G	T	C	AGAGATGA	(SEQ ID NO:204)
TGACTGTG	A	C	G	G	C	T	AGAGATGA	(SEQ ID NO:205)
TGACTGTG	A	C	G	G	C	C	AGAGATGA	(SEQ ID NO:206)
TGACTGTG	G	T	G	G	T	T	AGAGATGA	(SEQ ID NO:207)
TGACTGTG	G	T	G	G	T	C	AGAGATGA	(SEQ ID NO:208)
TGACTGTG	G	T	G	G	C	T	AGAGATGA	(SEQ ID NO:209)
TGACTGTG	G	T	G	G	C	C	AGAGATGA	(SEQ ID NO:210)
TGACTGTG	G	C	G	G	T	T	AGAGATGA	(SEQ ID NO:211)
TGACTGTG	G	C	G	G	T	C	AGAGATGA	(SEQ ID NO:212)
TGACTGTG	G	C	G	G	C	T	AGAGATGA	(SEQ ID NO:213)
TGACTGTG	G	C	G	G	C	C	AGAGATGA	(SEQ ID NO:214)
TGACTGTG	A	T	A	G	T	T	AGAGATGA	(SEQ ID NO:215)
TGACTGTG	A	T	A	G	T	C	AGAGATGA	(SEQ ID NO:216)
TGACTGTG	A	T	A	G	C	T	AGAGATGA	(SEQ ID NO:217)
TGACTGTG	A	T	A	G	C	C	AGAGATGA	(SEQ ID NO:218)
TGACTGTG	A	C	A	G	T	T	AGAGATGA	(SEQ ID NO:219)
TGACTGTG	A	C	A	G	T	C	AGAGATGA	(SEQ ID NO:220)
TGACTGTG	A	C	A	G	C	T	AGAGATGA	(SEQ ID NO:221)
TGACTGTG	A	C	A	G	C	C	AGAGATGA	(SEQ ID NO:222)
TGACTGTG	G	T	A	G	T	T	AGAGATGA	(SEQ ID NO:223)
TGACTGTG	G	T	A	G	T	C	AGAGATGA	(SEQ ID NO:224)
TGACTGTG	G	T	A	G	C	T	AGAGATGA	(SEQ ID NO:225)

5'	R	Y	α	β	Y	Y	3'	
TGACTGTG	G	T	A	G	C	C	AGAGATGA	<u>(SEQ ID NO:226)</u>
TGACTGTG	G	C	A	G	T	T	AGAGATGA	<u>(SEQ ID NO:227)</u>
TGACTGTG	G	C	A	G	T	C	AGAGATGA	<u>(SEQ ID NO:228)</u>
TGACTGTG	G	C	A	G	C	T	AGAGATGA	<u>(SEQ ID NO:229)</u>
TGACTGTG	G	C	A	G	C	C	AGAGATGA	<u>(SEQ ID NO:230)</u>
TGACTGTG	A	T	I	G	T	T	AGAGATGA	<u>(SEQ ID NO:231)</u>
TGACTGTG	A	T	I	G	T	C	AGAGATGA	<u>(SEQ ID NO:232)</u>
TGACTGTG	A	T	I	G	C	T	AGAGATGA	<u>(SEQ ID NO:233)</u>
TGACTGTG	A	T	I	G	C	C	AGAGATGA	<u>(SEQ ID NO:234)</u>
TGACTGTG	A	C	I	G	T	T	AGAGATGA	<u>(SEQ ID NO:235)</u>
TGACTGTG	A	C	I	G	T	C	AGAGATGA	<u>(SEQ ID NO:236)</u>
TGACTGTG	A	C	I	G	C	T	AGAGATGA	<u>(SEQ ID NO:237)</u>
TGACTGTG	A	C	I	G	C	C	AGAGATGA	<u>(SEQ ID NO:238)</u>
TGACTGTG	G	T	I	G	T	T	AGAGATGA	<u>(SEQ ID NO:239)</u>
TGACTGTG	G	T	I	G	T	C	AGAGATGA	<u>(SEQ ID NO:240)</u>
TGACTGTG	G	T	I	G	C	T	AGAGATGA	<u>(SEQ ID NO:241)</u>
TGACTGTG	G	T	I	G	C	C	AGAGATGA	<u>(SEQ ID NO:242)</u>
TGACTGTG	G	C	I	G	T	T	AGAGATGA	<u>(SEQ ID NO:243)</u>
TGACTGTG	G	C	I	G	T	C	AGAGATGA	<u>(SEQ ID NO:244)</u>
TGACTGTG	G	C	I	G	C	T	AGAGATGA	<u>(SEQ ID NO:245)</u>
TGACTGTG	G	C	I	G	C	C	AGAGATGA	<u>(SEQ ID NO:246)</u>
TGACTGTG	A	T	I	C	T	T	AGAGATGA	<u>(SEQ ID NO:247)</u>
TGACTGTG	A	T	I	C	T	C	AGAGATGA	<u>(SEQ ID NO:248)</u>
TGACTGTG	A	T	I	C	C	T	AGAGATGA	<u>(SEQ ID NO:249)</u>
TGACTGTG	A	T	I	C	C	C	AGAGATGA	<u>(SEQ ID NO:250)</u>
TGACTGTG	A	C	I	C	T	T	AGAGATGA	<u>(SEQ ID NO:251)</u>
TGACTGTG	A	C	I	C	T	C	AGAGATGA	<u>(SEQ ID NO:252)</u>
TGACTGTG	A	C	I	C	C	T	AGAGATGA	<u>(SEQ ID NO:253)</u>
TGACTGTG	A	C	I	C	C	C	AGAGATGA	<u>(SEQ ID NO:254)</u>
TGACTGTG	G	T	I	C	T	T	AGAGATGA	<u>(SEQ ID NO:255)</u>
TGACTGTG	G	T	I	C	T	C	AGAGATGA	<u>(SEQ ID NO:256)</u>
TGACTGTG	G	T	I	C	C	T	AGAGATGA	<u>(SEQ ID NO:257)</u>
TGACTGTG	G	T	I	C	C	C	AGAGATGA	<u>(SEQ ID NO:258)</u>
TGACTGTG	G	C	I	C	T	T	AGAGATGA	<u>(SEQ ID NO:259)</u>
TGACTGTG	G	C	I	C	T	C	AGAGATGA	<u>(SEQ ID NO:260)</u>
TGACTGTG	G	C	I	C	C	T	AGAGATGA	<u>(SEQ ID NO:261)</u>
TGACTGTG	G	C	I	C	C	C	AGAGATGA	<u>(SEQ ID NO:262)</u>
TGACTGTG	A	T	T	G	T	T	AGAGATGA	<u>(SEQ ID NO:263)</u>
TGACTGTG	A	T	T	G	T	C	AGAGATGA	<u>(SEQ ID NO:264)</u>
TGACTGTG	A	T	T	G	C	T	AGAGATGA	<u>(SEQ ID NO:265)</u>
TGACTGTG	A	T	T	G	C	C	AGAGATGA	<u>(SEQ ID NO:266)</u>

5'	R	Y	α	β	Y	Y	3'	
TGACTGTG	A	C	T	G	T	T	AGAGATGA	<u>(SEQ ID NO:267)</u>
TGACTGTG	A	C	T	G	T	C	AGAGATGA	<u>(SEQ ID NO:268)</u>
TGACTGTG	A	C	T	G	C	T	AGAGATGA	<u>(SEQ ID NO:269)</u>
TGACTGTG	A	C	T	G	C	C	AGAGATGA	<u>(SEQ ID NO:270)</u>
TGACTGTG	G	T	T	G	T	T	AGAGATGA	<u>(SEQ ID NO:271)</u>
TGACTGTG	G	T	T	G	T	C	AGAGATGA	<u>(SEQ ID NO:272)</u>
TGACTGTG	G	T	T	G	C	T	AGAGATGA	<u>(SEQ ID NO:273)</u>
TGACTGTG	G	T	T	G	C	C	AGAGATGA	<u>(SEQ ID NO:274)</u>
TGACTGTG	G	C	T	G	T	T	AGAGATGA	<u>(SEQ ID NO:275)</u>
TGACTGTG	G	C	T	G	T	C	AGAGATGA	<u>(SEQ ID NO:276)</u>
TGACTGTG	G	C	T	G	C	T	AGAGATGA	<u>(SEQ ID NO:277)</u>
TGACTGTG	G	C	T	G	C	C	AGAGATGA	<u>(SEQ ID NO:278)</u>
TGACTGTG	A	T	T	A	T	T	AGAGATGA	<u>(SEQ ID NO:279)</u>
TGACTGTG	A	T	T	A	T	C	AGAGATGA	<u>(SEQ ID NO:280)</u>
TGACTGTG	A	T	T	A	C	T	AGAGATGA	<u>(SEQ ID NO:281)</u>
TGACTGTG	A	T	T	A	C	C	AGAGATGA	<u>(SEQ ID NO:282)</u>
TGACTGTG	A	C	T	A	T	T	AGAGATGA	<u>(SEQ ID NO:283)</u>
TGACTGTG	A	C	T	A	T	C	AGAGATGA	<u>(SEQ ID NO:284)</u>
TGACTGTG	A	C	T	A	C	T	AGAGATGA	<u>(SEQ ID NO:285)</u>
TGACTGTG	A	C	T	A	C	C	AGAGATGA	<u>(SEQ ID NO:286)</u>
TGACTGTG	G	T	T	A	T	T	AGAGATGA	<u>(SEQ ID NO:287)</u>
TGACTGTG	G	T	T	A	T	C	AGAGATGA	<u>(SEQ ID NO:288)</u>
TGACTGTG	G	T	T	A	C	T	AGAGATGA	<u>(SEQ ID NO:289)</u>
TGACTGTG	G	T	T	A	C	C	AGAGATGA	<u>(SEQ ID NO:290)</u>
TGACTGTG	G	C	T	A	T	T	AGAGATGA	<u>(SEQ ID NO:291)</u>
TGACTGTG	G	C	T	A	T	C	AGAGATGA	<u>(SEQ ID NO:292)</u>
TGACTGTG	G	C	T	A	C	T	AGAGATGA	<u>(SEQ ID NO:293)</u>
TGACTGTG	G	C	T	A	C	C	AGAGATGA	<u>(SEQ ID NO:294)</u>
TGACTGTG	A	T	C	G	T	T	AGAGATGA	<u>(SEQ ID NO:295)</u>
TGACTGTG	A	C	C	G	T	T	AGAGATGA	<u>(SEQ ID NO:296)</u>

Please insert the accompanying paper copy of the Sequence Listing, page numbers 1 - 47, at the end of the application.